Turning heads to remember places

David Dupret & Jozsef Csicsvari

By eliciting a natural exploratory behavior in rats, head scanning, a study reveals that hippocampal place cells form new, stable firing fields in those locations where the behavior has just occurred.

One of the challenges of hippocampal research is to understand how place cells anchor their firing to specific locations in space. In this issue of *Nature Neuroscience*, Monaco *et al.*[1] provide new insights into this puzzle. They noticed that rats often engage in head-scanning during exploratory behavior. Other animals exhibit similar behaviors. For example, squirrels will rear and scan their surroundings when burying an acorn to ensure that they will be able to find it later. Surprisingly, Monaco *et al.*[1] found that hippocampal place representations can be altered following head scans: place cells can abruptly form new firing fields at a location where the rat has engaged in head scans before (**Fig. 1**). The new place cell firing emerged while animals foraged for food on a circular track. Head scanning at a given location predicted the emergence of new place fields during the subsequent pass. This work highlights the utility of analyzing ethologically relevant behavioral patterns and relating them to neuronal coding and circuit function. The findings of Monaco *et al.*[1] may facilitate future efforts to determine the sequential cascade of circuit events that are needed for the formation and stabilization of new place fields.

It has long been understood that the stereotypical rodent behaviors influence oscillatory patterns and the overall state of the hippocampus network[2]. Highly rhythmic theta-band oscillations (5–12 Hz) are present when animals actively engage in exploratory activity and locomotion. In contrast, theta oscillations disappear during waking behavioral inactivity, and intermittent 200-Hz oscillatory patterns called sharp waves/ripples (SWRs) emerge during this state[3]. SWRs are also present in certain conditions when animals are active; for example, they can be seen at goal locations and during grooming or eating.

Recently, interest has been drawn to other types of behavioral patterns as well, such as rearing and orienting responses. For example, rearing responses often occur when animals are exposed to novel environments[4], and it has been suggested that network activity during rearing may help stabilize new place maps. Hippocampal place cell firing has been also investigated during behavioral orienting responses that occur in mazes when an animal stops to decide which arm to take next. In these cases, during theta oscillations, the firing sequences of place cells often suggest the expression of alternative routes originating from the choice point[5]. It was suggested that these sequences may be related to decision-making processes. Even in the absence of theta oscillations, in behavioral delay periods, hippocampal population activity often encodes either the previous or the next path choices of the animal, or a combination of the two[6]. Moreover, place cell firing sequences occurring during SWRs in brief behavioral pauses may reflect the future trajectory of the animal[7], and this effect may diminish when animals are fully trained in a memory task[8].

Head-scanning behavior is known from ethological studies. It is typically observed in birds and is related to predator or prey scanning[9], but it has also been observed in rodents[2]. However, head scanning is less common in typical experimental conditions under which place cells are recorded, as animals are well-trained to forage for food without long pauses. Monaco *et al.*[1] recorded place cells while animals were searching for sporadic rewards on a circular track. Moreover, the researchers rotated local cues surrounding the track or introduced novel cues, thereby causing confusion between local cues near the track and distal cues elsewhere in the room. These experimental conditions ensured that the rats made a sufficient number of head scans to enable detection of the emergence of new place fields at locations where animals engaged in head scanning in the previous run. Previous work has identified certain conditions that lead to new place field formation, such as objects, environmental boundaries or reward[10,11]. However, no previous study has been able to link new place field formation to such a specific behavior of the animal.

This work illustrates the power of combined behavioral and electrophysiological analyses, highlighting that even brief behavioral patterns may have far-reaching consequences in circuit function. Rapid formation of new place fields during the course of the exploration session has been shown previously[10,12]. However, without detailed behavioral analysis it would not have been possible to identify a possible underlying cause for it. Similarly,

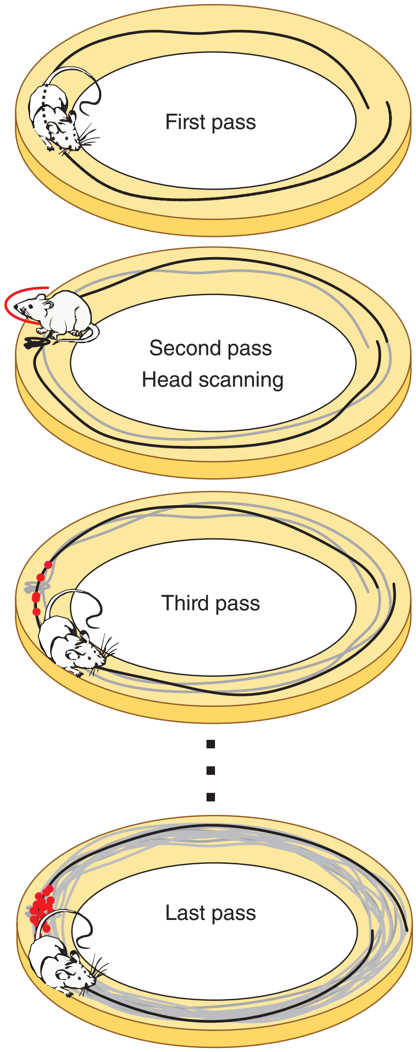

Figure 1 The firing of a place cell that develops a new place field at the location of a head scan. The black line illustrates the movement of the animals in the current pass; the gray lines show previous passes. Red dots mark locations at which the cell fires. The place cell starts to fire during the next pass after the head scan.

David Dupret is at the Medical Research Council Anatomical Neuropharmacology Unit, Department of Pharmacology, University of Oxford, Oxford, UK, and Jozsef Csicsvari is at the Institute of Science and Technology Austria, Klosterneuburg, Austria.
e-mail: david.dupret@pharm.ox.ac.uk or jozsef.csicsvari@ist.ac.at

behavioral analysis alone could not have deciphered a role for head-scanning behavior in altering hippocampal mnemonic representations of space.

What might the behavioral utility of head-scanning behavior be, considering the findings of this work? Head scanning often occurs at behaviorally important locations, such as at reward locations. Thus, head scanning may facilitate the reward-oriented remapping of place cells, which, in turn, would ensure a more accurate spatial code for those locations[11]. Furthermore, in some of the experiments by Monaco *et al.*[1], there was confusion introduced between near-track and distal room cues. During head scanning, animals may have stopped to orient themselves relative to distal cues. Hence, the formation of new place fields could help the animal to keep track of its location amid conflicting cues. Finally, it is important to note that stable place fields were formed within a single trial in this study. Such one-trial encoding of new place cells is a requirement of episodic memory; thus, this type of place cell might represent a substrate for this process.

Head scanning–related place field formation could also provide a useful tool for studying the network mechanisms behind the formation and stabilization of new place fields. New spatial maps form rapidly when animals enter a novel environment, leaving limited opportunity to collect sufficient data to investigate place field formation. In contrast, tasks that involve numerous head scans can enable investigators to study place field formation processes in multiple instances.

How is it that new place fields were formed so abruptly following head-scanning behavior? Recent work performing intracellular recording in freely moving animals has demonstrated that hippocampal cells often exhibit place-related depolarization of their membrane potentials[13]. This depolarization is often below spike threshold, but once cells are depolarized further by intracellular current injections, these cells start to fire action potentials at these locations. Moreover, they maintain firing at these locations later, even when no further depolarization is applied. Thus, it is plausible that extra depolarization during head scanning could trigger certain cells to form new place fields. Increased firing of cells in the CA3 region of the hippocampus during SWRs could be a source of the necessary depolarization[14]. An alternative depolarizing source could be the transient increase of nonspecific subcortical neurotransmitters. Indeed, acetylcholine levels may increase following head scanning, given that theta oscillatory power transiently increases at this time. Finally, a transient drop of interneuron firing rate noted during head scanning suggests that a transient disinhibition could also enable place cells to reach firing threshold during head scanning. Thus, as suggested for place field formation during other conditions[15], disinhibition could promote the development of new place fields during head scanning as well.

With the improvement of animal tracking methods and the development of machine vision algorithms to reconstruct the full body posture of animals, new avenues are opening to identify ethologically relevant behavioral patterns and relate them to circuit activity in the hippocampus and beyond. The recording of neuronal activity may further help to reveal new behavioral patterns or perhaps to divide existing patterns into subclasses on the basis of circuit activity patterns. The Monaco *et al.*[1] study provides a nice demonstration for the merit of such approaches by highlighting a role of head scans in the refinement of the hippocampal cognitive map of space.

COMPETING FINANCIAL INTERESTS

The authors declare no competing financial interests.

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Loss of phasic dopamine: a new addiction marker?

Daniele Caprioli, Donna Calu & Yavin Shaham

A study finds that the loss of phasic dopamine signal in ventral, but not dorsal, striatum predicts escalation of cocaine self-administration. We discuss the study's implications for addiction theory and treatment.

What is the role of dopamine in addiction? This question has been in the forefront of addiction research during the last four decades. During this time, numerous studies have implicated mesolimbic and nigrostriatal dopamine transmission in the rewarding effects of psychostimulant drugs and conditioned drug effects. In parallel, several prominent dopaminergic-centered addiction theories, which argue that dopamine transmission in ventral and/or dorsal striatum is critical for psychostimulant addiction[1–5], have emerged. These theories were primarily derived from studies using lesion, receptor pharmacology and microdialysis techniques that do not have the temporal resolution to assess the role of fast phasic dopamine transmission, which is critical to reward learning[5], in animal models of psychostimulant addiction. The development of fast-scan *in vivo* voltammetry to measure subsecond phasic dopamine release and the subsequent development of chronic implantable microsensors[6] to determine fluctuations in neurotransmitter release in behaving rodents over time have allowed Willuhn *et al.*[7] to address this question.

In a previous study[8], some of the same authors used the chronic implantable microsensor

Daniele Caprioli, Donna Calu and Yavin Shaham are in the Behavioral Neuroscience Research Branch, Intramural Research Program, National Institute on Drug Abuse, US National Institutes of Health, Department of Health and Human Services, Baltimore, Maryland, USA.
e-mail: yshaham@intra.nida.nih.gov